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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,780	07/22/2002	Christopher John Secombes	ABLE-0021	9521

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,780	SECOMBES ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55,58,60-63,65,66,68 and 70-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55,58,60-63,65,66,68 and 70-75* is/are rejected.

7)☒ Claim(s) *55,58,60-63,65,66,68 and 70-75* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's argument of 4/5/06 and corrected amendment of 7/13/06 are entered.

Claims 56, 64, and 69 are cancelled.

Claims 74-75 are newly added.

Claims 55, 63, 65, 68, and 73 are amended.

Claims 55, 58, 60-63, 65-66, 68, 70-75 are presently pending and considered.

Claim Status, Cancelled Claims

In light of the cancellation of Claims 56, 64, and 69, all rejections and/objections to such claims are rendered moot, and thus, are withdrawn.

Claim Objections

Claim 55 is objected to because of the following informalities:

Claim 55 recites the term "immunissation", however, proper spelling is "immunization".

Claim 55 recites the term "the fish", however, there are two fish references in the claim prior to the term "the fish", one drawn to a fish being treated, and the second drawn to a generic fish. While the Artisan would know that Applicant is claiming the fish being treated, proper English requires that Applicant amend the claim to refer to the fish being treated.

Claim 55 recites the limitation "N-end", however, the Artisan typically refers to such as the "N-terminus" of the polypeptide. While Artisan would know what Applicant is claiming, and hence, the claim is not rejected on this basis, Applicant is required to correct the claim to use the proper terminology.

Claim 60 recites the limitation "wherein the DNA encodes antibody molecules to several different epitopes", however, the only DNA sequence discussed is one encoding a single antibody. Such is not subject to a rejection for clarity however, because the Artisan would know Applicant is claiming that the plasmid also encodes such other antibodies.

Claim 61 recites the limitation "wherein the DNA sequence encodes a gene-expression library of antibodies". Similar to 60, this claim is objected for not properly claiming that the plasmid encodes these other antibodies.

Claim 68 recites the limitation "viral haemorrhagic septicaemia virus VHSV-neutralizing single chain antibody molecule". The term "VHSV" is an acronym for the viral haemorrhagic septicaemia virus, and hence, should be within parentheses, in order to denote that such term is not different from a simple viral haemorrhagic septicaemia virus, and further, the hyphen should be removed to note that such is not limited to the VHSV, but to the viral haemorrhagic septicaemia virus, also known as VHSV.

Claim 70 recites the limitation "wherein the DNA encodes antibody molecules to several different epitopes", however, the only DNA sequence discussed is one encoding a single antibody. Such is not subject to a rejection for clarity however, because the Artisan would know Applicant is claiming that the plasmid also encodes such other antibodies.

Claim 71 recites the limitation "wherein the DNA sequence encodes a gene-expression library of antibodies". Similar to 70, this claim is objected for not properly claiming that the plasmid encodes these other antibodies.

It is further noted that Claims 58, 60-63, 65-66, and 70-74 are necessarily objected to for depending from an objected-to base claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 – second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of the amendments, the rejections of Claims 55, 58, 60-63, 65-66, 68, and 70-73 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn, however, the amendments introduce the following new rejections.

Claims 55, 58, 60-63, 65-66, 68, and 70-75 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons necessitated by the amendments.

Claim 55 recites the limitation "upon administration of said construct in the form of purified plasmid DNA". The metes and bounds of such limitation are not clear. To wit, it is not clear, and further is inconsonant with the step of administration. The step of administration required simply requires administration of a plasmid, while the effect limitation, above, only requires expression and secretion if it is administered in purified form. Further, it is not clear whether Applicant is claiming one form of the method, wherein the plasmid is not purified, and no expression/secretion is required, and a second form of the method, wherein it is purified, expressed, and secreted.

Claim 55 recites the limitation "derived from the variable domains". The term "derived" is clear for its metes and bounds. To wit, for example, if the variable domains were mutated to form the variable domains of another antibody, would such still be encompassed by the claim?

Claim 63 recites the limitation "and further encodes a secretion signal of rainbow trout ...", however, from the specification and in light of the claim amendments, it is not clear whether Applicant wishes to claim a second secretion signal on the antibody, or whether such claim is meant to modify the secretion signal of the base claim.

Claim 63 also recites the limitation "derived from ...". Such term is so broad as to render the claim's metes and bounds indeterminate. To wit, is an antibody derived from another source, but equivalent to one derived from the recited antibody infringing? Also, such term indicates such breadth as to only require a portion of the recited material is used to derive any antibody, e.g., an amino acid used to make another antibody. Further, combining these aspects, it is clear that the claim encompasses anything under the sun.

Claim 68 recites the limitation "which are operably linked together ... and with the secretion signal". The metes and bounds of this limitation are not clear. To wit, it is not clear if the 3F1H10 antibody contains these linker and secretion signal sequence, or whether the antibody encoded by the plasmid contains such.

Claim 68 recites the limitation "and with the secretion signal". The metes and bounds of such limitation are not clear. To wit, it is unclear whether the secretion signal is with the linker, or separate. Further, if it is with the linker, it is unclear how the linker could link the other two sequences if it is on the N-terminus of the heavy chain, along with the operably linked secretion signal.

Claim 68 recites the limitation "derived from the variable domains". The term "derived" is clear for its metes and bounds. To wit, for example, if the variable domains were mutated to form the variable domains of another antibody, would such still be encompassed by the claim?

Claim 75 recites the term "the disease causing virus", however, the parent claim recites only VHSV, and as such, it is unclear what this term, and therefore, the whole claim refers to. To wit, is the antibody to a disease causing virus? Is VHSV any one of the viruses listed? Or is it the antibody being raised against such? Or is it something else? As such, the claim has not been further treated on the merits, except to include such claim in the rejections placed on its parent claims, as the Examiner cannot determine what Applicant is claiming.

Claim 73 recites the limitation "in the in the". The metes and bounds of such limitation are not clear.

Claim 73 recites the limitation "in the immunoglobulin heavy chain of the expressed antibody molecule". Such term lacks antecedent basis, as the heavy chain variable domain is what is being modified and expressed.

Claims 58, 60-63, 65-66, 70-75 are rejected for depending from a rejected base claim and not overcoming the lack of clarity in such base claim.

Response to Argument – Clarity

Applicant's argument of 4/5/06 has been considered with respect to the term "derived" because it is a similar ground of rejection, though due to the amendment, the exact basis is changed.

Applicant's argument has been fully considered and not found persuasive.

Applicant argues that by amending the claims to reflect the variable domains of the antibody, such overcomes the rejections (p. 10).

Such is not persuasive. Applicant's amendment simply changes the basis of the rejection, but not the core problem, the scope of the term is simply not defined, and could necessarily encompass anything derived from these domains through any method, as long as the starting material is that of the variable domains.

Claim Rejections - 35 USC § 112 – written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55, 58, 60-63, 65-66, 68, 70-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons necessitated by the amendments. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's claims encompass a generic single chain antibody derived from the variable heavy and variable light domains of an antibody raised against a fish-disease causing virus.

Applicant's specification, while providing antecedent basis for such terminology, e.g., pp. 3-5, and providing a specific mutation for a specific antibody (e.g., EXAMPLE 1), does not provide any description of how to mutate or other ways to derive such a generic single-chain

antibody from the variable light and heavy chains of an antibody raised against a disease causing virus.

Further, the Art provides no other support for Applicant's limitation, such that the Artisan would know how to derive these antibodies from these domains. To wit, it is well known that the variable domains of antibodies are the complementation-determining regions of the antibody, and therefore, even minor changes would introduce large changes in affinity, rendering the antibodies ineffective to bind their antigen. For example, Daugherty (2000) Proc. Natl. Acad. Sci., USA, 97(5): 2027-34 demonstrates that mutations to these regions generally lowers the affinity for antigen, albeit at a slower rate than expected (ABSTRACT).

Hence, at the time of invention, the Artisan would not have understood Applicant to have been possession of a generic single chain antibody derived from another antibody's variable domains, but only comprising such antibody's variable domains, as well as those specific mutations demonstrated.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55, 58, 60-63, and 65-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 55, and therefore, all its dependent claims, are drawn to the administration of purified plasmid. However, the specification provides not explicit or implicit support for such limitation.

Applicant argues that pages 5-8 and the examples provide support for such limitation (p. 9); however, the Examiner has found no such explicit or implicit support for such limitation, and further, the Examiner reviewed the specification and failed to find any other support.

Hence, these claims are rejected for comprising new matter.

Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55-56, 58, 60-66 and 68-73 remain, or are newly, rejected under 35 U.S.C. 112, first paragraph, for reasons record, because the specification, while being enabling for a composition for protection of a fish against viral haemorrhagic septicaemia virus (VHSV) comprising a non-infectious DNA nucleic acid construct encoding the single chain antibody 3F1H10 that recognizes VHSV, the DNA sequence for the antibody listed on pages 9-10 of the specification and which comprises substitutions of asparagines 35a with threonine and lysine 64 with threonine and is linked at the 5' end to the secretion signal of transforming growth factor beta, and which sequences is operably linked to the CMV promoter and a polyA tail for

protecting a fish against VHSV infection, and vaccines comprising such compositions, and methods of providing prophylactic treatment of fish against VHSV by the administration of these compositions, by injection into the epaxial muscles below the dorsal fin, which compositions transform cells of the muscle tissue local to the injection site and produce secreted 3F1H10 antibodies, thereby producing protection against VHSV, as well as the plasmid vector construct itself, does not reasonably provide enablement for a plasmid encoding any antibody, any secretion sequence, any promoter sequence, any form of administration, linker sequences comprising a secretion signal and being N-terminal to the antibody, any fish or any immunization to any fish-disease causing virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Due to Applicant's amendments, the rejection, while remaining the same, introduces new bases of rejection, i.e., the presence of an N-terminal linker comprising a secretion signal, and further any antibody derived from an antibody raised against a fish-disease causing virus.

With regard to the N-terminal linker comprising a secretion signal and being on the N-terminus of the antibody, the Artisan could not reasonably predict how this linker would operably link the two variable derived sequences, as the secretion signal must be N-terminal, and the linker, if also N-terminal to this region, would not link the variable sequences, as proteins are linear.

With regard to the breadth of antibodies derived from these variable regions, it is not reasonably predictable that any particular antibody derived would produce immunity to a virus, because such mutations and other derivations are not reasonably predicted to provide the

requisite binding, in view of the amount produced, as exacerbated by the promoter choices, in order to provide immunity. Such is generally discussed above, with regard to possession, and further exacerbated by Applicant's own art, which demonstrates that such binding affinity is crucial to the conferred immunity. To wit, Daugherty (2000) Proc. Natl. Acad. Sci., USA, 97(5): 2027-34 demonstrates that mutations to these regions generally lowers the affinity for antigen, albeit at a slower rate than expected (ABSTRACT), and Applicant's own art demonstrates that it is not reasonably predictable which mutations provide the requisite affinity, in the context of the levels of expression (Cupit (2001) Virus Res., 81: 47-56, p. 55, col. 2, last paragraph). Hence, it was not reasonably predictable which mutations, in any particular antibody domain, would produce the requisite activity to confer immunity.

Moreover, Applicant's specification and examples provide no more guidance than to rely on the art.

Hence, at the time of invention, the Artisan would have to experiment, on top of the experimentation at hand from the previous actions, to determine how to link two domains while the linker is in the N-terminus, and further, to experiment to determine which mutations of any particular domain could produce the requisite immunity in the context of any level of expression and secretion. Such experimentation is undue because it amounts to inventing Applicant's invention for Applicant, and hence, the claims are not enabled for their full scope.

Response to Argument – Enablement

Applicant's argument of 4/5/06 has been fully considered but is not found persuasive.

Applicant provides an analysis of the claims, but does not provide a demonstration of how such analysis overcomes the rejections provided, and hence, it is hard to address how these claims overcome the rejections (pp. 11-14).

For example, while it is admitted that Applicant has narrowed the scope of their claims, overcoming the aspects of any animal and any disease-causing virus by limiting such to fish and fish-disease causing viruses, such only narrows the scope rejected, but fails to change the scope which is enabled.

Claim Rejections - 35 USC § 102 – old rejections, Chang

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's arguments, the rejections of Claims 1, 15, 21, and 34 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,543,144 to Chang, filed 21 January 1993; date of patent 6 August 1996, are withdrawn.

It is noted that due to typographical error, the Examiner did not remove this rejection in the Official Action of 10/5/05, however, such rejection is not applicable to the claims as were present in the prior Official Action, much less the currently-claimed invention.

Claim Rejections - 35 USC § 103 – Duan

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendment and argument, the rejections of Claims 55-56, 58, 60-62, 64-66, and 68-72 under 35 U.S.C. 103(a) as being unpatentable over WIPO Doc. No.: WO 96/37234 to Duan, et al., Filed 23 May 1996, Published 28 November 1996, are withdrawn.

To wit, while Duan does recognize the possibility of passive immunization, as taught by Applicant, it is clear that the prior Art did not recognize passive immunization as claimed by Applicant was reasonably predictable. For example, Kalinke, et al. (1996) Eur. J. Immunol., 26: 2801-06 demonstrates the use of a specific antibody to protect against VSV, but also recognizes that their results are inconsistent with those obtained with yellow fever virus (p. 2806, col. 1). Hence, there exists a lack of a reasonable expectation of success due to a lack of reasonable predictability that any particular sc-Ab could be so delivered and successfully passively immunize a fish against any particular virus. Therefore, such amounts to an invitation to try, and, consistent with the enablement rejection, above, these claims are not obvious.

Conclusion

No Claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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